

Commentary

Monocyte and Macrophage Reactions

by Steven D. Douglas*

For a number of years we have been working with monocytes and macrophages, and I would like to direct my remarks to a number of questions concerning the properties of the monocyte and the macrophage. I think it is quite evident that the mononuclear phagocyte has a major role in dealing with particles.

I would like to start out by raising two questions: whether the particles are free particles or whether the particles have adsorbed to them materials, either proteins or ions, which they have acquired from the fluid phase upon entry (a factor which would have obvious implications concerning subsequent handling of the particle by the phagocytic cell) and the relationship of the particle to alterations in erythrocytes and the possible effect of erythrocytes in *in vivo* systems.

I thought it would be worthwhile to specifically mention a number of recent properties of the monocyte-macrophage which may have bearing on the questions being discussed this afternoon. First, recent studies primarily from Rabinovitch's laboratory at NYU (1) have demonstrated a spreading phenomenon: namely, that a reversible spreading of the mouse macrophage occurs. In the past few months, we have demonstrated the same phenomenon with the human blood monocyte. A number of materials induce spreading. These include antigen-antibody complexes and proteolytic enzymes such as subtilisin; in addition, manganese

is one of the most potent inducers. The question of the relationship between macrophage spreading and its influence on subsequent events is an area which needs further work.

I would like also to mention plasma membrane receptors on the monocyte-macrophage which at this stage of our knowledge can be divided into two types: nonimmunologic recognition, which one would think is the mechanism with which we are dealing here, and immunologic recognition, which we have been studying. The immunologic recognition by these cell types is very specific (2). With human immunoglobulins two of the four kinds of human immunoglobulins are recognized by the human macrophage. These are IgG₁ and IgG₃. There is a separate and independent recognition system for the third component of complement. As a corollary to this—if particles do have immunoproteins bound to them—this would completely alter the way that the phagocytic cell would deal with them.

Finally I wanted to mention the various factors which have been described immunologically which are produced by macrophages or to which the macrophage responds. The blood neutrophil is known to produce a chemotactic factor to which monocyte-macrophages respond and which leads to migration of monocyte macrophages. Antigen-stimulated lymphocytes are known to produce migration inhibitory factor which has now been at least partially characterized by David and Bloom (3, 4). In addition there appeared to be factors produced by macrophages which influence lymphocytes, and these factors may have implications in how par-

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ticles are dealt with. Finally, the cytotoxic properties of the macrophages are of particular interest and have been currently studied very intensively in terms of the ability of macrophages to kill target cells of a number of kinds in tumor systems with or without antibodies. This cytotoxic potential has been described and been shown to be quite distant from the T-cell-mediated destruction of tumor cells and also distinct from the bone-marrow lymphocyte destruction of tumor cells. This potential could lead to the release of factors from the macrophage perhaps leading to the kinds of events which Harington described (5).

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